UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/127,624	08/03/98	PONCE DE LEON F	002076-007

021839 HM12/0516
BURNS DOANE SWECKER & MATHIS
P O BOX 1404
ALEXANDRIA VA 22313-1404

EXAMINER	
CLARK, D	
ART UNIT	**PAPER NUMBER**
1633	7

DATE MAILED: 05/16/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/127,624	Ponce De Leon et al.
Examiner	**Group Art Unit**
Deborah Clark	1633

☒ Responsive to communication(s) filed on *Apr 3, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 2, 4, 5, 7, 8, 10-13, 15, 16, 18-20, and 22-28* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 4, 5, 7, 8, 10-13, 15, 16, 18-20, and 22-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Applicant's amendment and response to the prior office action has been received, 04/03/00, paper no. 6. Claims 1, 2, 4, 5, 7, 8, 10-13, 15, 16, 18-20, and 22-28 are now pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 11-13, 15, 16, 18, and 25-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to method of making transgenic chimeric avians or transgenic chimeric avians. The specification does not adequately describe the claimed invention. The specification describes making a chimeric avian and prophetically states that one could introduce a nucleic acid into PGCs to make a transgenic chimeric avian. However, specification does not describe any construct for use in making transgenic avian. Further, when PGCs were transfected, the transfection was not stable and was reported to be transient. In view of this statement one of

skill in the art would not reasonably conclude that applicants were in possession of a method to make transgenic avians or transgenic avians themselves. "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." (See UC vs. Eli Lilli, (CA FC) 43 USPQ2d 1398). It is concluded that the description of the claimed subject matter does not convey that the inventor had invented the claimed invention.

4. Claims 15 and 16 stand, and newly amended or presented claims 11-13, 18, and 25-28 are rejected under 35 USC 112, 1st paragraph for reasons or record as set forth previously in regards to claims 14-17.

Applicants traverse the rejection. First applicants note that claim 14 has been canceled and it's limitations incorporated into claim 1. However, it is noted that claim 1 is not directed to a method of making chimeric avians. It appears that applicants intended to refer to claim 11.

Applicants point out that the discussion on pages 3-5 reflect the deficiencies of the prior art in particular from the lack of long term culture methods and that the art had not failed in producing chimeric or transgenic avians. Applicants continue to state that the goal was to develop a long term culture system for avian PGCs, not to produce a transgenic or chimeric avian. However, that is actually what is being claimed. Further, it is noted that now not only the methods, but also the chimeric avian is being claimed. These claims are not enabled for reasons discussed in the previous office action. Further, in regards to pages 3-5, the examiner did not state that the making of transgenic or chimeric avians was impossible, but rather that success had been limited. Applicant's discussion on pages 3-5 clearly reflects this position.

Applicants submit the reference Vick et al. and state that it was known that transgenic chimeric birds could be made using transformed PGCs. This reference is noted, however, the reference is not taken as enabling for making a transgenic chimeric avian following culturing of the PGCs and using any non-retroviral vector. Vick et al. do not discuss the expression of the transgene or any phenotype conferred by expression of the transgene. Claims 15 and 16 require that the nucleic acid be a therapeutic nucleic acid. Claims 27 and 28 are directed to a transgenic chimeric avian. The instant specification nor the prior art enables the claimed invention because, as set forth and supported in the previous office action, the making a transgenic avians is not predictable. It is not clear that the transgene would be expressed to any level to allow recovery of the protein or to confer any phenotype to the birds which would enable their use. Applicants have not taught any particular construct to use for expression of the transgene nor has any transgenic

chimeric avian been demonstrated. As pointed out previously, "The specification does not provide any working example which demonstrates the production of a chimeric bird where the PGCs were transfected with a nucleic acid. In fact, applicants tried and were unsuccessful in stably maintaining transfected PGCs. The PGCs were transiently transfected with a marker gene for the purpose of maintaining a selectable phenotype (see page 30). Applicants reported that only 1/50 PGCs were transfected and could not be stably maintained. Therefore, it is not clear that the gene would be expressed in a transgenic bird because the transfection was transient". It is not clear whether applicant's method of culturing or the transgene design contributed to this lack of stable transfection. However, in order to make a transgenic bird, stable transfection is required. Because applicants have not taught any construct which would result in stable transfection, the prior art is not considered to enable the claimed invention.

Lastly, applicants allege that the examiner has rejected the claims because of deficiencies in the prior art. The specification must enable the claimed invention. The specification must teach that which was not known in the prior art. In this case, the specification does not compensate for the deficiencies of the prior art. Further, it is noted that the state of the art and it's lack of predictability are proper factors to consider in making a rejection based upon a lack of enablement under 35 USC 112, 1st paragraph. Applicants also state that the prior art had made transgenic avians, but with much more difficulty in the absence of the present invention. The present invention does not preclude the previous difficulty because transgenic avians could not be

made using transiently transfected PGCs. The specification does not teach how to stably transfect PGCs nor how to make a transgenic avian using transiently transfected PGCs.

Applicants argue that the specification need not teach what is well known in the art and that working examples are not required. However, the making of transgenic avians using transfected PGCs is not sufficiently well known in the art. Further, the presence of working examples is a factor which is properly relied upon in considering whether a claimed invention is enabled.

Applicants argue that the examiner was contradictory to herself regarding the amount of experimentation required for successful transfection. However, this is not the case. The claims rejected are not solely directed to transfecting PGCs, but to making a transgenic avian or a transgenic avian. Further, the mechanics of transfecting PGCs is known. What is not known is using transfected PGCs to make a transgenic avian.

Applicants argue that prior persons of ordinary skill were not deterred from making transgenic avians even though they could not culture the cells to ensure transfection. However, the prior persons used only a particular vector which was not taught by applicants to result in making the transgenic avians. Further, it was not taught in the prior art as to whether the transgene was detectably expressed or to which effect it had upon the bird. Therefore, it remains that it would require undue experimentation for one of skill in the art to make a transgenic avian using the teaching provided in the specification.

5. Claims 1, 2, 4, 5, 7, 8, 10, 19, 20, and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of transfecting PGCs or an improvement in the method of transfecting PGCs.

The claims are not enabled because the specification teaches a method for culturing PGCs. However, the claims are directed to a method of transfecting PGCs. The specification states that PGCs were transfected, but only transiently. The instant specification does not enable one of skill in the art to use transiently transfected PGCs. The specification teaches only one method to use the PGCs, for making a transgenic bird. For reasons discussed above, this method is not enabled. Because the making of a transgenic bird requires stable transfection, and because applicants method results only in transient transfection, it is concluded that it would require undue experimentation to use the claimed invention.

6. Claims 1, 2, 1, 5, 7, 8, 10-13, 15, 16, 18, and 22-28 stand or are rejected under 35 USC 112, 2nd paragraph for reasons of record and as discussed below.

Claim 1 continues to recite the phrase "prolonged time period". Apparently applicants intended to delete this recitation, however, it is noted that the recitation remains in line 14.

Claims 1, 11, and 22 recite the phrase "desired nucleic acid". This phrase renders the claims indefinite because the meets and bounds of the claims cannot be ascertained. It is not clearly set forth what makes a nucleic acid desired.

Claim 2 now has parenthesis following the growth factors. It is not clear as to whether these amounts are to be taken as a limitation or not. Therefore, the claims are indefinite.

Claim 23 is indefinite because it depends upon itself. The claim has been examined as though it depends from claim 22 as it appears as though that is what applicants intended.

Double Patenting

7. The previously made provisional rejection over claims 1, 2, 4, 5, 11-13, and 18 is held in abeyance as requested by applicants until such time that the claims are indicated as allowable. The claims stand provisionally rejected as set forth previously.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 19, 20, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Vick et al.

Claims 19 and 20 are directed to transfected PGCs. Claim 27 is directed to a transgenic avian. Vick et al. discloses transfected PGCs and transgenic avians. Therefore, the claims are anticipated. The claims are product-by-process claims. See MPEP 2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe , 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). It is noted that the cells are not cultured for 14 days, however, this step does not add any particular property to the cell or the avian. Therefore, the end product, the cells or the avian, are no different from those disclosed by Vick et al.

Claim Rejections - 35 USC § 103

10. Claims 11, 12, 13, 18, 22, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vick et al. in view of Pain et al.

Vick et al. teach a transgenic avians and a method of making transgenic avians using transfected PGCs (see entire article). The claims require the steps of isolating a pure population of PGCs, maintenance with 4 particular factors, transfection with a desired nucleic acid, allowing the recipient avian to develop into a bird and selecting chimeric avians that express the phenotype

conferred by the desired nucleic acid. Vick et al. disclose each of the steps excluding maintenance in the 4 particular factors.

Pain et al. teaches maintaining a culture comprising PGCs in medium comprising the 4 factors. One of skill in the art would have been motivated to use the factors disclosed by Pain et al. for maintaining the PGCs disclosed by Vick et al. because Pain et al. teach that the cells were cultured in an undifferentiated state for more than 160 days (see page 2345, column 2). One of skill in the art would be motivated to maintain the PGCs in a medium that would allow them to remain undifferentiated.

Therefore, it would have been *prima facie* obvious at the time the invention was made to modify the method to by Vick et al. to include the medium disclosed by Pain et al. for any period of maintenance.

It is noted that none of the rejected claims requires any particular time period for culturing in the steps of the claims.

Conclusion

11. No claim is allowed.

12. Claims 1, 2, 4, 5, 7, 8, and 10 are free of the prior art of record because the claims require that a pure population of PGCs be cultured for 14 days. The prior art did not teach or fairly suggest that PGCs could be cultured for this period of time without differentiating. Claims 15, 16, 23, 24, 26, and 28 are free of the prior art because the claims require the use of a

therapeutic polypeptide. The prior art does not teach or fairly suggest that any such polypeptide would be expressed to any detectable level following transfection of PGCs.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Clark whose telephone number is (703) 305-4051. The examiner can normally be reached on Mondays-Fridays from 7:10 a.m. EST to 3:40 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Deborah Clark

DEBORAH J. CLARK
PATENT EXAMINER